Rearrangements of tricyclic ketones: [3.3.3]propellane formation via a γ-enolate revealed in an approach to the pentalenene skeleton through β-enolization[1]

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This paper is dedicated to Professor David B. MacLean in recognition of his contributions to chemistry

HEMANT A. PATEL, J.B. STOTHERS, and S.E. THOMAS. Can. J. Chem. **72**, 56 (1994).

The known isomerization of the tricyclo[5.3.1.$0^{1,5}$]- to the [6.3.0.$0^{1,5}$]undecane skeleton by β-homoenolization led to examination of 2,9,9-trimethyl-6-methoxymethyltricyclo[5.3.1.$0^{1,5}$]undecanone (**6**) as a potential precursor for the synthesis of pentalenene, a naturally occurring sesquiterpenoid, utilizing a β-enolate rearrangement as a key step. While the anticipated rearrangement of **6** occurs, it is a minor process. The major rearrangement product arises by generation of a γ-enolate intermediate from a tricyclic enone formed by loss of methanol from **6**. This constitutes a new route to [3.3.3]propellanes and provides a third example of γ-enolate rearrangement. Structures of the products were established primarily from their ^{1}H and ^{13}Cmr spectra.

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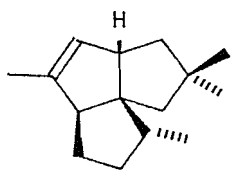
L'isomérisation connue du squelette tricyclo[5.3.1.$0^{1,5}$]undécane en tricyclo[6.3.0.$0^{1,5}$]undécane par β-homoénolisation a conduit à examiner l'utilité de la 2,9,9-triméthyl-6-méthoxytricyclo[5.3.1.$0^{1,5}$]undécanone (**6**) comme précurseur potentiel dans la synthèse du pentalènène, un sesquiterpénoïde naturel, en utilisant le réarrangement β-énolique comme étape clé. Même si le réarrangement désiré du produit **6** se produit, il s'agit d'un processus mineur. Le produit majeur de réarrangement provient d'un intermédiaire γ-énolique formé à partir de l'énone tricyclique **6**, par la perte de méthanol. Cette réaction constitue une nouvelle voie de préparation des [3.3.3]propellanes et fournit un troisième exemple d'un réarrangement γ-énolique. Les structures des produits ont été principalement déterminées à partir de leurs spectres rmn du ^{1}H et du ^{13}C.

[Traduit par la rédaction]

Introduction

Over the past 15 years, several naturally occurring sesquiterpenoids with various angular triquinane carbon skeletons have been discovered (1). These compounds have attracted attention as targets for synthesis not only because of their inherently interesting structures but also since some possess biological activity. Two examples having the tricyclo[6.3.0.0]undecane ring system are pentalenene (**1**) (2) and isocomene (**2**) (3). Pentalenene is the biosynthetic precursor of the pentalenolactones (4), antibiotic metabolites produced by several *Streptomyces* species, and it has been synthesized by several groups through a variety of routes (1, 5). Isocomene cooccurs with the first carbocyclic propellane to be found in nature, modhephene (**3**) (6). Several syntheses of these fascinating structures have been described: isocomene (1, 7) and modhephene (8).

Our interest in the potential of β-enolate rearrangement as a preparative route to less accessible polycyclic carbon skeletons has led to a synthesis of the linear triquinane, hirsutene (9), and to the generation of the angular triquinane ring system through the rearrangement **4** → **5** (10). From this finding, we became interested in devising a sequence leading to **1** from an appropriate analog of **4**. To this end, ketone **6** was selected as a suitable compound for an initial investigation, with the interconversion **6** → **7** envisaged as the key step. We found that this reaction indeed occurs, but only as a minor process. The major rearrangement involves an unsaturated derivative of **6** and leads to the generation of a [3.3.3]propellane. We wish to describe here the results of our study of the behavior of **6** under typical homoenolization conditions (*t*-BuO^{-}/*t*-BuOH/185°C).



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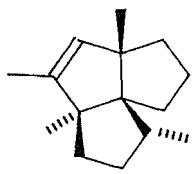

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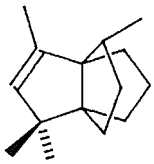

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Results

Syntheses

The sequence employed for the preparation of ketone **6** is given in Scheme 1. The key step involves a well-known intramolecular Diels–Alder reaction (11) to furnish the [5.2.1.0] skeleton, which is then readily expanded to the required [5.3.1.0] system of **6**. The reaction of 2-methyloxetane (12) with methyl propargyl ether (13), as described by Yamaguchi et al. (14), gave 7-methoxyhept-5-yn-2-ol (**8**) in 88% yield. Hydrogenation of **8** over the Lindlar catalyst afforded 7-methoxy-*cis*-hept-5-en-2-ol (**9**) in 93% yield. Tosylation of **9** and condensation of this tosylate with sodium cyclopentadiene fur-

[1]Part 146 of the series ^{13}Cmr studies; for Part 145 see ref. 33.
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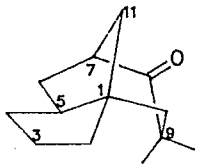

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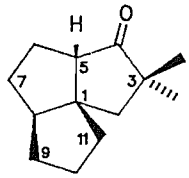

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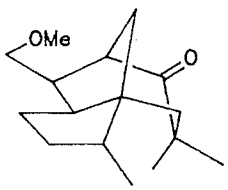

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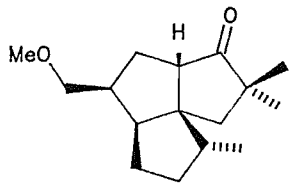

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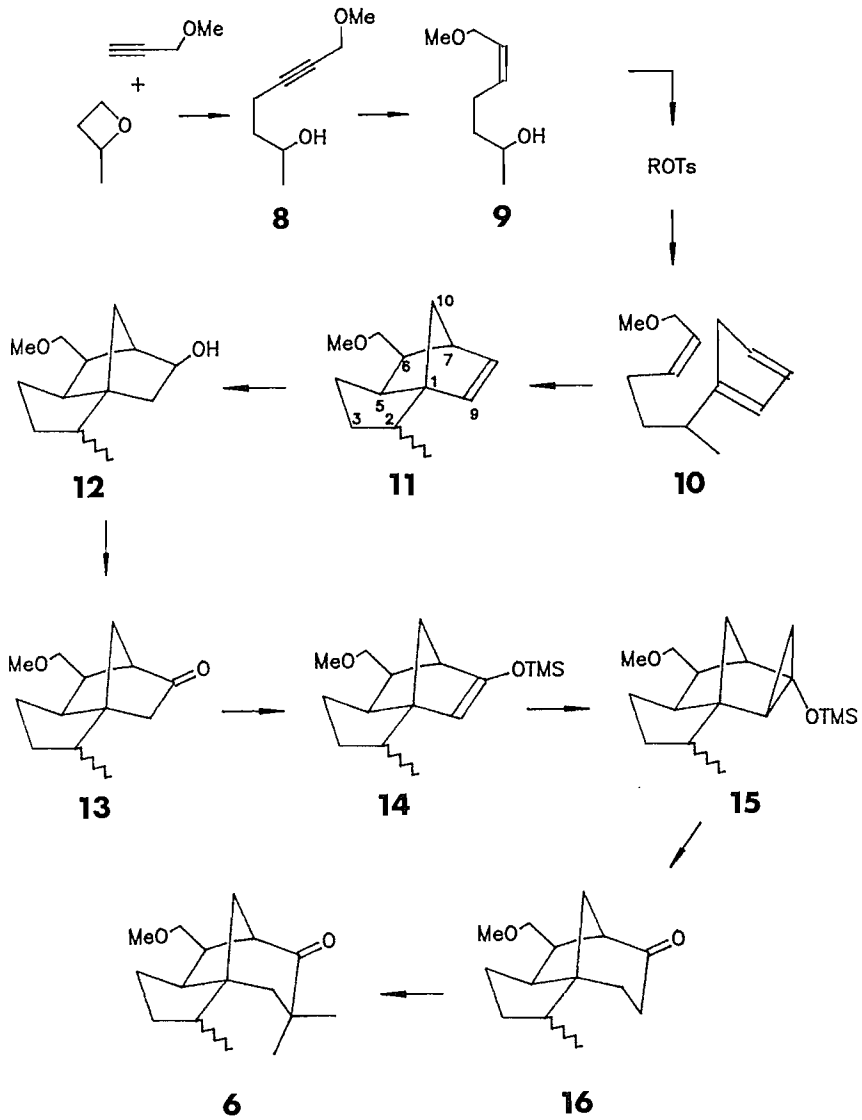
nished a 5:3 mixture of two trienes in 84% yield.The ^{13}Cmr spectrum contained four methylene signals for each component, with only that at δ_C 68.0 (-CH_2O-) common to both, showing that **10** and its 3′-isomer were present. The cyclopentadienyl methylene proton bands, δ 2.925 (m, $\nu_{1/2}$ 4.5 Hz) and δ 2.845 (m, $\nu_{1/2}$ 4.1 Hz) with relative intensities of 5:3, respectively, indicated that **10** was the major component. In any event, the assignment was not critical since the intramolecular Diels–Alder cycloaddition proceeded in 82% yield to the desired [5.2.1.0] olefin **11** as a 2:1 mixture of the 2-epimers.

An excellent analogy for the transformation of **9** to **11** has been described by Breitholle and Fallis in the report of their synthesis of cedrol and cedrene (15). Their key step was the intramolecular Diels–Alder reaction of 1,5-dimethyl-4-hexenyl-2′-cyclopentadiene, prepared from sodium cyclopentadiene and 1,5-dimethyl-4-hexenyl tosylate. Although they obtained a single alkylcyclopentadiene isomer, in contrast to our results, they stressed that the Diels–Alder conditions may alter the equilibrium mixture of these isomers and, consequently, all



SCHEME 1

TABLE 1. 2-Methyl and skeletal methylene ^{13}C shieldings for **6**, **11–14**, and **16**[a]

Compound	Epimer	2-Me	C-3	C-4	C-9	C-10	C-11
11	Major	20.0	37.2	25.1		49.3	
	Minor	17.2	34.8	23.3		42.8	
12	Major	18.9	36.4	23.8	41.8	36.0	
	Minor	15.9	34.4	22.1	43.1	29.3	
13	Major	18.7	36.1	24.2	46.3	39.1	
	Minor	15.6	33.6	22.4	46.9	32.8	
14	Major	19.9	36.3	24.9		47.7	
	Minor	16.9	34.3	23.1		41.2	
16	Major	16.3	36.1	25.2	35.4	32.0	41.7
	Minor	14.7	(33.8)	23.3	34.7	36.0	(33.9)
6[b]	Major	16.3	35.7	24.9		46.9	38.6
	Minor	14.6	33.1	23.5		49.1	31.1

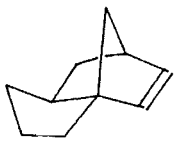
[a]In ppm from TMS for $CDCl_3$ solutions; values in parentheses may be reversed.
[b]Full data are given in Table 3; for the others, see Experimental.

possible intramolecular cycloaddition products should be considered. They concluded that the formation of the [5.2.1.0] skeleton would be expected to be strongly favored, as was observed in their case and in the present study. The isomeric internal Diels–Alder structures were excluded by the nmr spectra of the products in each of these studies. A second feature of this cycloaddition is the lack of a simple method to control the stereochemisty at C-2. In their synthesis of the cedrane skeleton, Breitholle and Fallis obtained a 1:1 mixture of the 2-epimers of the Diels–Alder cycloadduct but a 2:1 mixture of the 2-epimers of **11** was found in this work.

Hydroboration of **11** with $Siam_2BH$ in THF proceeded smoothly to give **12** in 74% yield; this was subsequently oxidized with pyridinium chlorochromate (16) to furnish **13** in 95% yield. Ring expansion to the desired [5.3.1.0] ring system was accomplished in a three-step sequence that had been demonstrated for several polycyclic ketones (17). Conversion of **13** to enol ether **14** (90%), cyclopropanation of **14** to **15** (81%), and ketonization in 88% yield gave **16** as a 2:1 epimeric mixture. Dimethylation of **16** with $MeI/NaNH_2/Et_2O$ proceeded in 80% yield to furnish **6**, as a 2:1 mixture of the 2-epimers, for our homoenolization experiments.

Consideration of the methylene shieldings in the ^{13}C spectra of these compounds led to a rational stereochemical assignment for the 2-methyl group in these epimeric pairs. Specific assignments for the individual carbons in **11–14** were made by comparing the shift data with the results for the compounds lacking the 2- and 6-substituents (10). The shifts for the 2-methyl and the skeletal methylene carbons in **11–14** are collected in Table 1.

In each of the sets of three methylene signals for **11** and **14**, those near 35 and 24 ppm could be readily assigned to C-3 and C-4, respectively, by comparison with the data for **17** and **18**. While the corresponding signals for the latter appear near 25 and 33 ppm, respectively, the 2-methyl group in **11** and **14** will deshield C-3 by ca. 9 ppm through its β-effect and the *exo*-6 methylene group will shield C-4 appreciably because these carbons are *syn*-periplanar. As a result, the C-3 and C-4 shieldings are reversed in **11** and **14**. The shifts for the third methylene signal, arising from C-10, differ by 6.5 ppm for each pair of epimers, which must reflect the orientation of the 2-methyl group. This group is either *syn* or *anti* to C-10 in the two epimers and, in the *syn* form, will exert a shielding effect thereon because of the relatively small dihedral angle relating the two centres. Analogous trends are also found for **12** and **13**



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(see Table 1). A consistent difference of ca. 3 ppm is observed for the 2-methyl carbons in each epimeric mixture. In each pair, the minor form exhibits the more shielded 2-methyl and C-10 signals, and we can conclude, therefore, that the epimer having an *anti*-2-methyl group is predominant in each of these mixtures.

Assignments for these carbons in **6** and **16** are included in Table 1. These were also made by comparisons with the data for **4** and the parent ketone for which unequivocal assignments were available (10). For the two epimers of **6**, the C-11 shieldings differ by 7.5 ppm and, consequently, we can conclude that the desired *anti*-2-methyl epimer is the major form.

Homoenolization experiments

With the epimeric mixture of **6** in hand, we proceeded with our examination of its behavior under homoenolization conditions. After treatment of **6** with *t*-BuO^-/*t*-BuOH at 185°C for periods ranging from 24 to 240 h, we obtained neutral products in 53–80% yields by pentane extraction. Extraction of the aqueous phase after it was acidified furnished a single acidic product in 17–41% yields. The neutral fraction contained five major tlc spots; samples of each spot were examined by ^{13}Cmr to find that only partial separation had been achieved. Gas–liquid chromatographic (glc) analysis showed that the product contained two groups of components, a group of four having distinctly shorter retention times than a second group of three. The relative proportion of the first group slowly increased with reaction time, constituting ca. 75% of the neutral product after 240 h.

In the second group, two of the bands appeared to arise from two poorly resolved compounds and one, which slowly decreased with time, was easily shown to be the starting material. The first of the three bands was more symmetric and increased slowly to contain ~7% of the total neutral product after 240 h. ^{13}C spectra of samples collected by preparative glc indicated the presence of two closely related compounds in a 10:1 ratio. The major component, having a molecular formula

TABLE 2. ^{13}C shieldings for **5**, **7**, and *epi*-**7**[a]

Carbon	**5**	**7**	*epi*-**7**	Carbon	**5**	**7**	*epi*-**7**
1	55.5	58.3	58.1	9	33.3	22.8	24.7
2	50.9	43.5	49.5	10	27.0	35.0	35.6
3	47.5	47.5	47.5	11	43.2	44.1	44.9
4	225.9	225.6	225.6	3-CH_3	24.7	24.7	25.6
5	60.2	58.2	55.1		26.6	26.4	27.1
6	29.6	31.8	34.6	7-CH_2		74.0	73.7
7	33.4	42.3	42.6	11-CH_3		17.4	14.9
8	53.3	53.3	52.0	OCH_3		59.0	58.9

[a]In ppm from TMS for $CDCl_3$ solutions.

TABLE 3. ^{13}C shieldings for **6**, **19**–**21**[a]

	6		**19**		**20**		**21**	
Carbon	Major	Minor	Major	Minor	Major	Minor	Major	Minor
1	54.9	56.6	54.6	57.0	54.8	55.5	58.6	58.7
2	41.0	41.1	40.6	41.2	41.3	41.8	41.8	37.6
3	35.7	33.1	36.5	33.0	33.5	32.2	36.7_3	36.6_7
4	24.9	23.5	25.1	23.2	32.1	31.3	21.6	21.9
5	43.7	44.7	47.5	47.1	50.1	51.9	154.1	153.0
6	48.1	48.2	37.8	38.7	154.9	155.9	126.7	127.3
7	56.2	55.1	49.0	48.0	61.3	61.1	66.4	65.0
8	217.3	217.5	80.0	80.1	214.5	214.5	215.2	215.0
9	42.1	42.3	35.2	35.3	43.1	43.2	43.0	43.3
10	46.9	49.1	47.3	50.2	46.9	48.9	39.0	40.7
11	38.6	31.1	42.3	33.9	40.5	33.3	45.2	47.2
2-CH_3	16.3	14.6	16.8	15.2	17.1	14.1	13.9	16.5
9-CH_3	31.3	31.2_7	24.1	24.0	30.2	30.1	30.7_6	30.8_0
	31.4	31.2_2	35.3	35.0	32.7	32.5	34.0	33.9
6-CH_2X	73.4	73.3	75.0	75.1	108.7	108.5	13.2	13.5
CH_3O	58.5	58.4	58.7	58.7				

[a]In ppm from TMS for $CDCl_3$ solutions.

of $C_{16}H_{26}O_2$ by precise mass measurement, is an isomer of **6** with a cyclopentanone ring to judge from its carbonyl absorption (1730 cm^{-1}, δ_C 225.6); this is quite different from that for **6** (1700 cm^{-1}, δ_C 217.3, 217.5). From nmr spectra, the major compound was identified as **7**, accompanied by small amounts of its *syn*-2-methyl epimer. These were anticipated to form by β-enolate rearrangement of **6**. The results from $^{13}C\{^1H\}$ and $^1H\{^1H\}$ correlation spectra allowed complete assignments for the ^{13}C signals arising from **7**. Three ^{13}C methyl signals at δ_C 24.7, 26.4, and 59.0 correlated with ^1H singlets at δ 1.02, 1.06, and 3.28, respectively, while the highest field peak at δ_C 17.4 correlated with the proton doublet (δ 0.98, J = 7.0 Hz, 11-Me) coupled to H-11 (δ 1.98, m), which, in turn, is coupled to the 10-methylene protons near 1.4 and 1.6 ppm; these patterns correlate with the ^{13}C peaks, δ_C 44.1 (C-11) and 35.0 (C-10), respectively. An AX pattern, δ 2.17, δ 1.45, J_{AX} = 14.1 Hz, was readily assigned to the 2-methylene protons, which correlated with the methylene signal at δ_C 43.5 (C-2). The lowest field ^1H methine pattern at δ 2.28 (bd, J = 9.1 Hz), coupled to a methylene group near δ 1.4 and 2 .0, served to identify C-5 and -6, δ_C 58.2 and 31.8, respectively. The fourth methylene carbon signal, δ_C 22.8, arises from C-9. The ^{13}C data are collected in Table 2 with those for the minor component, *epi*-**7**, and **5**. From these data, it is clear that C-9 is strongly shielded by the methylene carbon on C-7, as expected since these are *syn*-periplanar. The shifts for C-2 in **7** and for C-5 in *epi*-**7** differ markedly from the corresponding shieldings in **5**. In **7**, C-2 is shielded by 7.4 ppm and C-5 by 5.1 ppm in *epi*-**7** relative to the values for **5**. This must reflect the orientation of the 11-methyl group and is only consistent with **7** bearing an *anti*-11-methyl group, i.e., *syn*-periplanar to C-2.

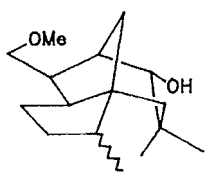
Preparative glc provided samples of the third band, which was found to contain a 2:1 mixture of alcohols. The ^{13}C spectrum showed these to be closely related to the starting material, LAH reduction of which gave an identical mixture. Therefore, these must be **19**; the ^{13}C data are listed in Table 3. Reduction of **6** was puzzling because the carbonyl group is unaffected under these conditions in the vast majority of ketones so far examined (18). To our knowledge, the only exceptions are 3-phenyl-6,6-dimethylcyclohexanone and its cycloheptanone analog from which small amounts of alcohols are formed under these conditions (19); but these are rather different systems.

For Bands 1–4 in order of increasing retention time in the first group, samples for characterization were obtained by preparative glc. Each was a mixture of epimers, but the relative proportions in two of these samples differed markedly from that of the initial ketone. All were found to have lost the methoxyl group and to contain one double bond. Band 3 constituted about 5% of the neutral product from short runs, while Band 2 was prominent in all samples, exhibiting a maximum of ~30% (72 h) and then decreasing to about 8%. Band 1 grew slowly to constitute about 45% of the total neutral product after 240 h, whereas Band 4 was a minor component in each of the product mixtures.

Band 3, which showed little change in relative intensity with time, consisted of a 2:1 epimeric mixture of ketones, each component of which gave rise to nmr signals for three methyl groups and those for an exocyclic methylene group. This showed that the methoxyl group had been lost, while the carbonyl absorption (δ_C 214.5) indicated that no major skeletal change had occurred. An identical mixture was prepared from the initial ketone by treatment with NaI/Me_3SiCl in MeCN (20), to replace the methoxyl group with iodide, followed by reaction with base to eliminate HI. Thus, this product was assigned structure **20** with which the ^{13}Cmr data are fully consistent; these may be compared with those for **6** (see Table 3). The replacement of C-6 with an sp^2 carbon produced marked shifts for C-5, C-6, C-7, and C-11, as expected, and the -3 ppm shift for the carbonyl signal is consistent with the formation of a β,γ-enone (21).

Band 2, a major product in the early neutral samples, was found to contain a 4:1 mixture of epimeric ketones from its ^{13}Cmr spectrum. It is isomeric with **20**, having a molecular formula of $C_{15}H_{22}O$ by precise mass measurement. The nmr spectrum of each epimer included signals for four C-methyl groups, one of which is olefinic (δ_H 1.57, δ_C 13.2, 13.5), together with those for two nonprotonated sp^2 carbons (δ_C 126.7, 154.1 and 127.3, 153.0). As in **20**, the carbonyl absorption at δ_C 215.0 and 215.2 indicated that no major skeletal change was involved. This product, therefore, was assigned structure **21** on the basis of the ^{13}C data (see Table 3).

Since **20** and **21** must be related through a common allylic anion, additional evidence for these structures was sought by examination of the behavior of **20** in strong base. After treatment of **20** at 130°C with *t*-BuO–/*t*-BuOH for 24 h, the neutral fraction contained only **20** and **21** in a 4:1 ratio, and after 72 h this ratio was 1:1. This confirmed that **20** and **21** differ only in the position of the olefinic bond. For the neutral product, the



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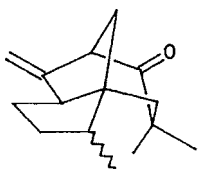

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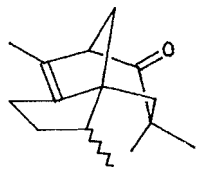

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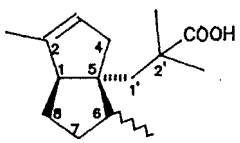

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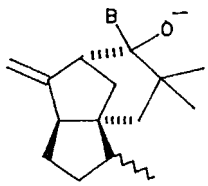

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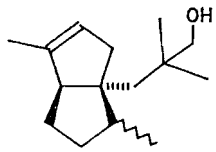

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yields were 51 (24 h) and 43% (72 h) and, for the acid, 38 and 46%, respectively. The ^{13}C spectrum of the acidic product was virtually identical to that for the acidic fraction from the homoenolization experiments with **6**. Both contained two sets of 15 signals, ascribable to a pair of epimeric acids. The proportions of these acids differed slightly in the two cases, with a slight excess of one in the runs with **6**, but essentially equal proportions from **20** and **21**. From the ^{13}C spectra, each has a trisubstituted double bond, four methyl groups, of which one is olefinic, four methylene, two methine, and two quaternary carbons, as well as the carboxyl group. These data are consistent with structure **22**, which can arise from **20** and (or) **21** through Haller–Bauer cleavage after addition at the carbonyl carbon by the alkoxide base, collapse of which could generate an allylic anion (see **23**). Although this is one of a number of possible isomers, differing only in the position of the double bond, **22** must be the most stable. It may be noted that earlier studies had shown that *tert*-butyl esters do not survive under these reaction conditions and the corresponding acids are isolated. Assignment of the ^{13}C signals for the **22** epimers was made by comparison with the data for several model compounds (22) and by heteronuclear $^{13}C\{^1H\}$ correlation spectra. The ^{13}C data are collected in Table 4 and the ^{1}H data are in the experimental section.

The spectra of samples from Band 4 were strikingly similar to those exhibited by **22**, except that the carboxyl signals were replaced by those for hydroxymethyl carbons. Identical spectra were recorded for samples obtained by LAH reduction of **22**. Thus, this product is **24**; the ^{13}C data are collected in Table 4. The stereochemistry of the 6-methyl group in each epimeric pair **22** and **24** was revealed by the large difference found for the C-1′ shieldings. The upfield signal must arise from the *exo* epimer in which the 6-methyl is *syn*-periplanar to C-1′. Thus, these mixtures **22** and **24** contained a small excess of the *exo* epimer.

Band 1 increased slowly with reaction time to represent about 45% of the total neutral product after 240 h. Its ^{13}C spectrum revealed the presence of two epimers, in a 10:1 ratio, which gave rise to carbonyl absorption (1730 cm^{-1}, δ_C 224.0, 225.0) indicative of cyclopentanone rings. Exact mass measurement gave a molecular formula of $C_{15}H_{22}O$. For each of the two epimers, the ^{13}C spectrum included signals for two olefinic carbons of a trisubstituted double bond, and those for four methyl, of which one is olefinic, four methylene, one methine, and **three** quaternary carbons. With the ^{1}H, $^1H\{^1H\}$, and $^{13}C\{^1H\}$ COSY

TABLE 4. ^{13}C shieldings for the *exo*- and *endo*-6-methyl isomers of **22** and **24**[a]

	22		24			22		24	
Carbon	*exo*	*endo*	*exo*	*endo*	Carbon	*exo*	*endo*	*exo*	*endo*
1	55.5	59.1	58.9	56.3	2-CH_3	14.9	15.3	15.4	15.6
2	143.6	141.7	143.6	142.7	6-CH_3	13.0	14.3	14.2	14.5
3	121.0	123.7	124.1	121.7	1′	41.1	50.1	39.9	48.1
4	43.3	39.3	43.8	39.2	2′	53.8	55.4$_5$	54.6	56.1
5	42.3	42.4	36.2	37.2	2′-CH_3	24.1	26.7	25.0	25.4
6	46.3	44.1	46.5	45.4		29.4	27.4	26.1	25.6
7	32.7	32.9	32.7	32.9	COOH	186.2	186.4		
8	27.8	28.9	28.1	29.2	CH_2OH			74.0	73.5

[a]In ppm from TMS for $CDCl_3$ solutions.

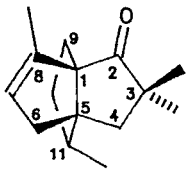
TABLE 5. ^1H and ^{13}Cmr data for **25** and *epi*-**25**[a]

	25			*epi*-25	
	^1H	^{13}C		^{13}C	
Position	In $CDCl_3$	In $CDCl_3$	In C_6H_6	In $CDCl_3$	In C_6H_6
1	—	76.7	76.7		77.3
2	—	224.0	221.7	225.0	222.3
3	—	48.5	48.3	47.4	47.2
4	1.556 [13.5] 1.650 [13.5]	42.8	42.8	49.7	49.8
5	—	56.8	56.9	58.5	58.5
6	2.370 [2.2, 2.4, 17.0] 2.454 [2.2, 2.4, 17.0]	46.6	46.7	41.2	41.4
7	5.080 [1.4, 2.2]	123.7	123.5	126.1	125.9
8	—	143.0	143.5	140.7	141.2
9	1.42 [6.0, 12.5, 12.5] 2.02 [6.8, 12.5]	35.1	35.3	34.5	34.7
10	~1.0 [m] ~1.6 [m]	33.6	33.7	33.5	33.8
11	~1.65 [m]	47.2	47.4	45.5	45.7
3-CH_3	0.974	25.2	25.5	27.9	28.0
	1.053	27.0	27.0	28.6	28.6
8-CH_3	1.67 [1.4, 2.4]	12.9	13.0	13.1	13.2
11-CH_3	0.976 [6.4]	12.0	12.0	13.7	13.7

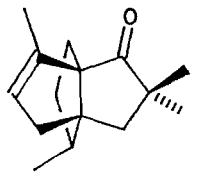
[a]Shieldings in ppm from internal TMS; ^1H–^1H couplings in Hz listed within square brackets.

spectra, all protons of the major component were assigned and correlated with the carbon signals; from these data three structural subunits were identified.

The olefinic methyl protons (δ 1.67) exhibited allylic coupling to the olefinic proton (J = 1.5 Hz) and homoallylic coupling to a pair of methylene protons (J = 2.4 Hz) with which the olefinic proton is coupled (J = 2.2 Hz). These interactions, confirmed by decoupling, established the presence of a -CH_2-CH=C(CH_3)- unit. Methyl protons (δ 0.976, d, J = 6.4 Hz) coupled to a methine proton, which is also coupled to one of a pair of contiguous methylene groups, revealed a -$(CH_2)_2$-CH(CH_3)- unit. A $^{13}C\{^1H\}$ flock spectrum (23) showed that the methyl protons giving rise to singlets at δ 0.974 and 1.053 are both vicinally coupled to a methylene carbon whose protons appear as an AB pattern (δ 1.556, 1.650, J_{AB} = 13.5 Hz). Thus, a -$CH_2C(CH_3)_2$- unit was identified. The combination of these three units with the two quaternary centres and the carbonyl led to the propellene structures **25** and *epi*-**25** for these compounds. The ^1H and ^{13}C results for **25** are given in Table 5 with the ^{13}C results for *epi*-**25**. Within the strong proton spectrum of **25**, only the signals for H-7 (δ 5.24), the 3- and 11-methyl groups (δ 1.031, s; 1.073, s; 0.945, d, J = 6.4 Hz), and an AB system (1.71, 1.98, J = 13.7 Hz) for *epi*-**25** were easily discerned. Further, this AB system was correlated with the δ_C 49.7 signal in the $^{13}C\{^1H\}$ COSY spectrum, thereby identifying C-4 in *epi*-**25**. Since the C-4 shieldings will depend on the orientation of the 11-methyl group and C-4 absorbs at δ_C 42.8 in **25**, we conclude that the 11-methyl is *syn*-periplanar to C-4 in **25**, in which C-4 is shielded by –7 ppm. The C-6 shieldings also support this assignment, since these exhibit the opposite trend. The shift of +5.4 ppm for C-6 in **25** is consistent with an *anti*-periplanar relationship to the 11-methyl group.



25



epi-**25**

TABLE 6. Composition[a] of the product mixtures from **6**

Time (h)	Neutral Fraction[b] 6	7	19	20	21	24	25	Acid fraction 22
24	42	8	3	2	21	<2	2	17
72	10	5	7	5	30	3	7	25
120	8	6	6	2	20	8	12	31
144	7	5	5	3	20	6	15	34
240	2	7	5	<2	8	6	24	41
120[c]	8	8	8	5	27	4	10	20
240[c]	6	10	10	<1	12	2	15	36

[a]Given as the proportion, on a % molar basis, of isolated product.
[b]Estimated from a combination of glc and ^{13}Cmr data.
[c]Results from runs with the pure major epimer (see text).

The composition of the product mixtures from the experiments with **6** are listed in Table 6. These data include the results for a few runs with pure samples of the major epimer of **6**, small quantities of which were obtained by repeated chromatography over silica. The latter data confirmed that the major component in each epimeric mixture arose from the major epimer of **6**.

To shed more light on the sequence of formation of the neutral products, samples of **21** were treated with *t*-BuO$^-$/*t*-BuOH. The neutral fraction, isolated in 85% yield after 100 h at 150°C, was found to be virtually identical to the starting material, according to the ^{13}C spectra. At 185°C, glc analysis showed that **21** was transformed slowly to **25** and *epi*-**25** together with small amounts of unidentified neutral material. The mixture of propellenones constituted ca. 25 and 60% of the neutral fraction after 50 and 150 h, respectively. From the results of the experiments with **20** and **21**, it became clear that the sequence is **20** → **21** → **25** + *epi*-**25**. In principle, each of these is prone to Haller–Bauer cleavage leading to **22** since this process will generate an allylic carbanion, as noted above (see **23**). The results indicate, however, that **20** is the most susceptible to this cleavage, and the propellenones the least. It can be noted that **24** was not found in the products from the experiments with **20** or **21**.

Discussion

By analogy with our earlier findings for **4** (10, 24), we would anticipate β-proton abstraction from **6** at C-6 and -11 to generate the β-enolates **26** and **27**, or equivalent species, respectively. Cleavage of these β-enolates can proceed by either, or both, of two modes: *a* and *b* in Scheme 2. Path *a* regenerates starting material and *b* leads to rearranged product. For the corresponding β-enolates from **4**, the cleavage is unidirectional, since **5** is the only rearranged product (10) and H/D exchange was observed at C-6 but not at C-11 (24). The isolation of **7** and *epi*-**7** showed that proton abstraction proceeded at C-11 in **6** to form **27**, or its equivalent, with subsequent opening to the tricyclo[6.3.0.0]undecanone skeleton. In agreement with earlier results for **4**, there was no evidence of formation of the [4.3.2.0] system **28**, but, in sharp contrast, rearrangement to **7** is not a major mode of reaction for **6**.

Four neutral products from **6** lack the methoxyl group and contain an olefinic bond. This can be envisaged to involve an E1cB process through an "open" β-enolate, such as **29**, leading to **20**, as shown in Scheme 2. It should be noted that β-enolates are commonly depicted as cyclopropoxide ions as a convenient symbolism. Although results for many β-enolate rearrangements are readily accommodated by these species, the cyclopropoxide form may be a representation of the transition state between rapidly equilibrating "open" forms. Precise definition of β-enolates is difficult. In any event, isomerization **20** → **21** would involve abstraction of H-5, generating the allylic carbanion **30**, and protonation at the incipient methyl carbon to form **21**. Our data provide permissive evidence that **21** is the more stable. Introduction of the double bond through loss of the methoxyl renders both **20** and **21** susceptible to Haller–Bauer cleavage because collapse of the intermediates **31***a* and **31***b*, formed by addition of alkoxide ion at the carbonyl carbon, will give an allylic anion. The isolation of **22** indicates that the isomers differing only in the position of the double bond must be less stable.

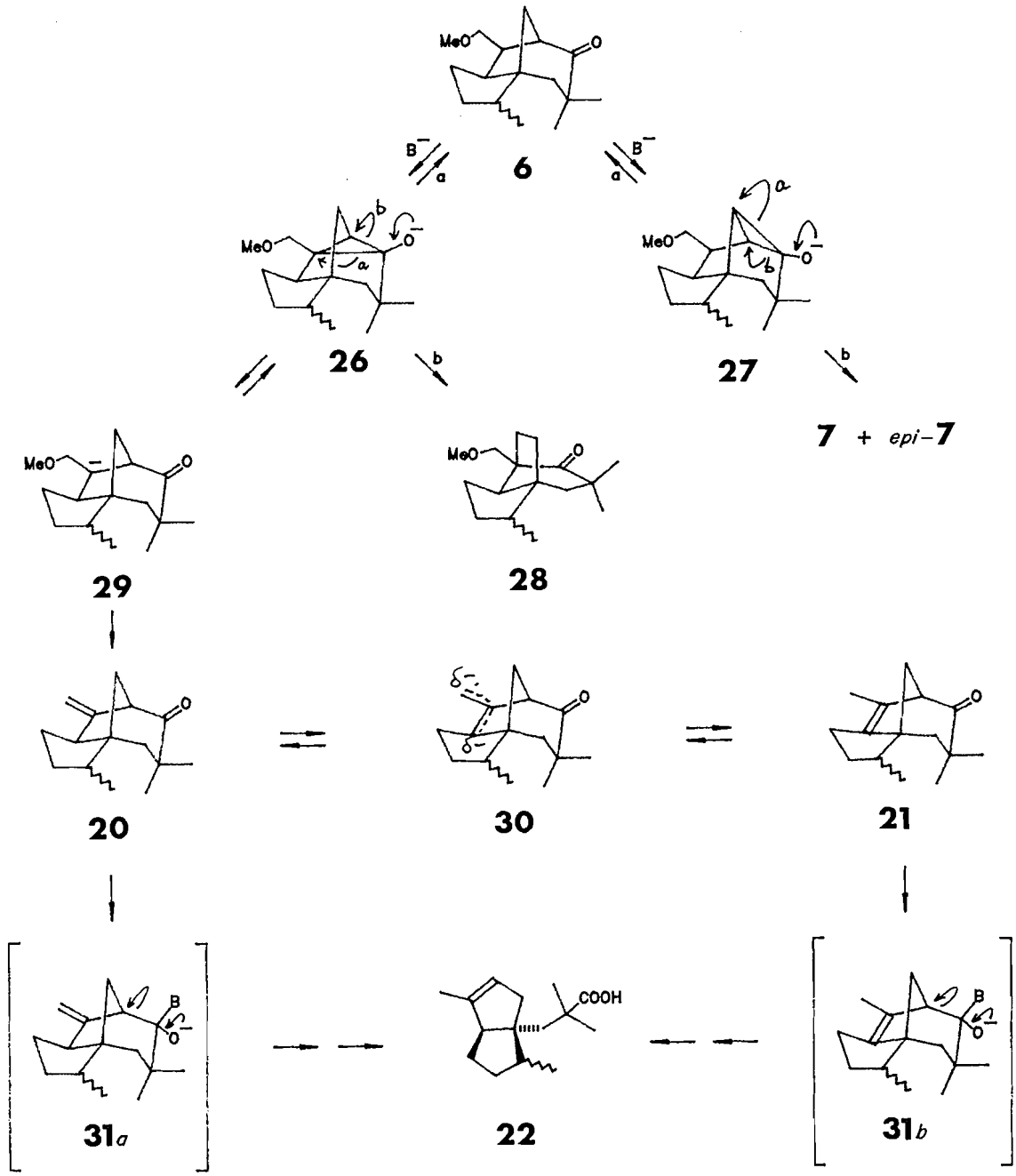
Although the original objective of this study was doomed by the disappointingly low yields found for the interconversion **6** → **7**, the unexpected finding that **25** is the major rearrangement product was a welcome surprise for two reasons. The isolation of **25** not only illustrates a new route to the [3.3.3]propellane skeleton but it also provides an example of γ-enolate rearrangement, since its formation is readily rationalized in terms of **32**, or an equivalent species, formed from **20** and **21**, as outlined in Scheme 3. Cleavage of **32** by path *b* leads to **33**, which will equilibrate with **25** (*epi*-**25**) under the strongly basic conditions. Since **33** was not detected in the neutral product mixtures, this equilibrium clearly favors the skeleton having the endocyclic double bond.

Since the discovery that a ketonic carbonyl group can activate proton abstraction from carbons other than those to which it is directly bonded (25), the vast majority of the reported cases involve β-enolate formation (18). However, ^{1}H/^{2}H exchange studies have shown that γ-enolization occurs in a few systems (18), but rearrangement had been observed in only two cases (26, 27). Thus, the formation of **25** from **20** and **21** is a third example of γ-enolate rearrangement.

Although both **20** and **21** may undergo β-enolization to form tricyclo[6.3.0.0]undecenones **36***a–c*, it is conceivable that these were destroyed by Haller–Bauer cleavage to **22** (see Scheme 4).

The fate of **21** is distinctly different from that of its simpler analog **34**, which we had investigated earlier (28). The major neutral product from **34** was **35**, showing that the anticipated β-enolization at C-8 produced the [3.3.0] skeleton, but subsequent reduction of the olefinic bond had not been anticipated. Furthermore, the rest of the neutral product consisted of compounds having a *tert*-butoxyl group, showing that the addition of *t*-BuO– to the double bond in **34** is a competitive process. None of the products that would arise by the corresponding processes with **21** was detected.

An analogous competitive reduction process has been encountered in one other study in which it was found that **37** is reduced to **38** (27) under these conditions. We have ascribed the formation of both **35** and **38** to single electron transfer from *tert*-butoxide anion to the conjugated carbonyl group. A distinctly different reduction process was recently observed (19) in another homoenolization study in which it was found that **39** is reduced slowly to the corresponding alcohol. We suggested that this process may be initiated by formation of **40** through homolytic cleavage of the more substituted bond in the cyclic β-enolate formed from **39**, by analogy with the observation that **41** and **42** are in rapid equilibrium (29) and the fact that an oxy anion substituent has a significant weakening effect on the adjacent bonds (30). In any event, other reduction processes must be operative in the present system to produce **19** and **24**.



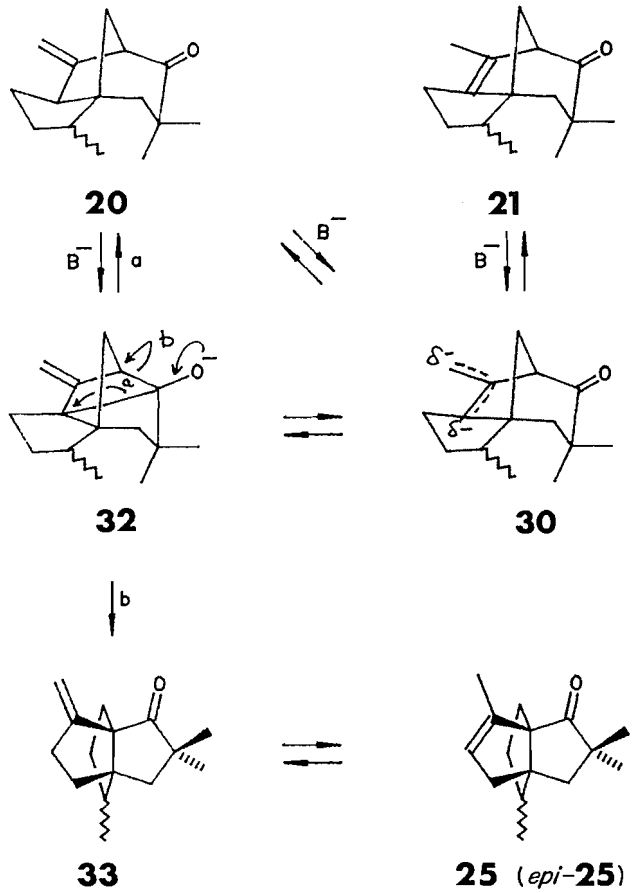
SCHEME 2

Alcohol **19** must arise simply from reduction of the carbonyl group in **6**. This process can be attributed to hydride transfer from the methoxide ion formed through the E1cB elimination in anion **29** (Scheme 2). The failure to detect formaldehyde is not surprising since it would have been easily lost during the work-up.

Alcohol **24** is a minor component in all of the neutral product mixtures from **6**, but was not found in the products obtained upon the same treatment of **20** or **21**. This observation leads us to suggest that its formation is triggered by hydride transfer from methoxide ion to the carbonyl group in **20** and (or) **21**. Subsequent cleavage of the resultant alkoxide through a retro-aldol reaction, as outlined in Scheme 5, would yield bicyclic aldehyde **43**, which could undergo a Cannizzaro reaction to give equimolar quantities of **22** and **24**. From the experiments with **20** and **21** as starting material, there is no doubt that **22** is primarily generated by their Haller–Bauer cleavage.

Experimental

Gas–liquid chromatography (glc) was carried out on a Varian 3300 instrument using a column of 5% SE-30 on Chromosorb W 80-100. Thin-layer chromatography (tlc) was done on Kiesel gel 60 F_{254} plates and flash chromatography (FC) columns were prepared as described in the literature (31). Tetrahydrofuran (THF) and ether were distilled from Na/benzophenone just before use. Pyridine, *tert*-butyl alcohol, diisopropylamine, and trimethylamine were distilled from CaH_2 and stored over 4A molecular sieves.



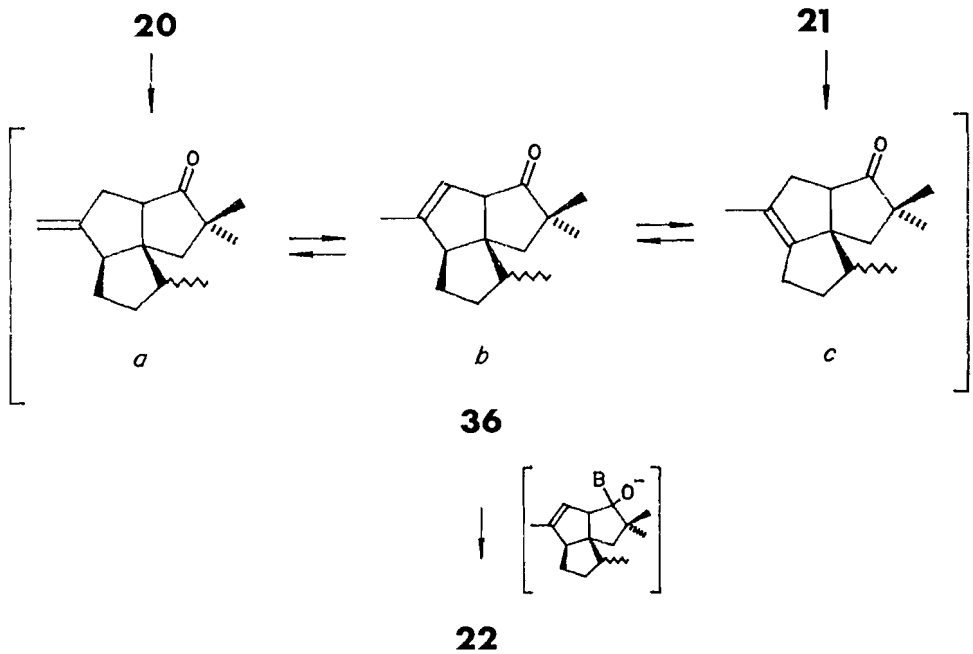
SCHEME 3

Infrared spectra were recorded with either a Beckman 4250 instrument or a Bruker/IBM FTIR 32 spectrophotometer. Mass spectra were obtained with either a Varian MAT-311A or a Finigan MAT 8230 instrument at 70 eV for routine spectra and at 20 eV for exact mass measurements.

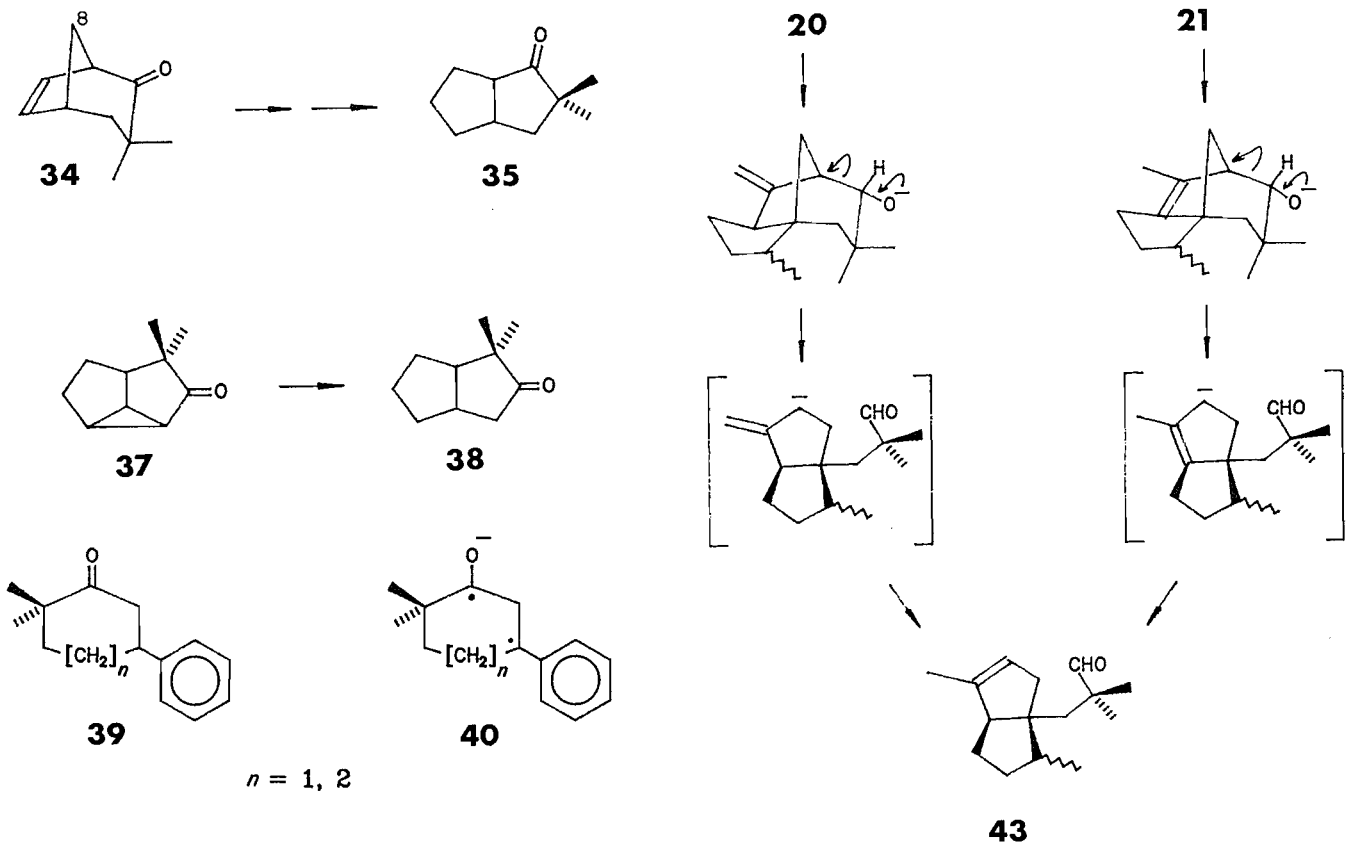
Proton and carbon nmr spectra of each compound were obtained with Varian XL-200 (^{1}H) and XL-300 (^{13}C) spectrometers. The number of protons bonded to each carbon was found by recording either the APT or DEPT spectrum. Correlation spectra were obtained using the programs of the Varian software, $^1H\{^1H\}$ and $^{13}C\{^1H\}$ spectra with the HOMCOR and HETCOR sequences, while long-range $^{13}C\{^1H\}$ correlations were revealed with spectra recorded using the FLOCK sequence (23). While full assignments for the ^{13}Cmr spectra are presented, the fact that most of the compounds were obtained as C-2 epimeric mixtures precluded complete analysis of their ^{1}Hmr spectra, thereby limiting definitive assignments to those listed.

7-Methoxy-5-heptyn-2-ol (8)

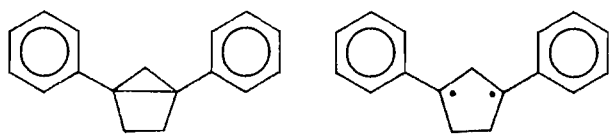
To a stirred solution of methyl propargyl ether (13) (3.5 g, 0.05 mol) in THF (100 mL) under dry nitrogen was added *n*-BuLi (19.2 mL, 2.6 M in hexane) at –78°C. Stirring was continued for 20 min, before the sequential addition of 2-methyloxetane (12) (1.8 g, 0.025 mol) and $BF_3{\cdot}Et_2O$ (7.5 mL) at –78°C. This mixture was stirred at –78°C for 0.5 h before it was allowed to warm to room temperature and diluted with saturated NH_4Cl solution. After the product was extracted with ether (3 × 60 mL), the extracts were washed with brine, 10% $NaHCO_3$ solution, and brine again, before drying over anhydrous Mg_2SO_4. Removal of the solvent furnished a yellow oil. Distillation was attempted but led to decomposition; thus, the product was purified by FC (EtOAc – petroleum ether, 40:60) to furnish alcohol **8** (3.1 g, 88% yield); ir ($CDCl_3$): 3640, 3480 (OH), 2840 (OMe), 2240 (C≡C), 1090 (C—O) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 1.10 (d, 3H, J = 6.1 Hz, H-1), 1.55 (dt, 2H, J = 6.1, 7.2 Hz, H-3), 2.25 (tt, 2H, J = 2.1, 7.2 Hz, H-4) 2.48 (s, OH), 3.26 (s, 3H, OMe), 3.81 (tq, 1H, J = 6.1, 6.1 Hz, H-2), 3.97 (t, 2H, J = 2.1 Hz, H-7); ^{13}Cmr ($CDCl_3$) δ: 23.2, 57.2 (2 × CH_3), 15.2, 37.5, 60.0 (3 ×



SCHEME 4



SCHEME 5



41 42

CH_2), 66.6 (CH), 75.9, 86.5 (C≡C). Exact Mass calcd. for $C_7H_{10}O$ (M – 32): 110.0732; found: 110.0736.

7-Methoxy-cis-*5-hepten-2-ol (9)*

A solution of alcohol **8** (0.67 g, 4.72 mmol) in THF – petroleum ether (20:80, 60 mL) containing 0.4 mL of pyridine and the Lindlar catalyst (135 mg) was hydrogenated at –15°C until one equivalent of H_2 was taken up. The progress of the reaction was also monitored by tlc. When the reaction was deemed complete, the catalyst was removed by filtration and the solvent evaporated. The residue was taken up in ether (100 mL) and the ethereal solution washed with 3% aqueous HCl and brine before drying over anhydrous $MgSO_4$. Evaporationof the solvent afforded **9** as a yellow oil (0.61 g, 93%): ir ($CHCl_3$): 3640, 3450 (OH), 3045 (=CH), 2840 (OMe), 1450 (C=C), 1100 (C—O) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 1.08 (d, 3H, J = 6.3 Hz, H-1), 1.35–1.50 (m, 2H, H-3), 2.05–2.25 (m, 2H, H-4), 2.80 (bs, 1H, OH), 3.24 (s, 3H, OMe), 3.70 (tq, 1H, J = 6.3, 6.4 Hz, H-2), 3.8–4.0 (m, 2H, H-7), 5.4–5.6 (m, 2H, H-5,6); ^{13}Cmr ($CDCl_3$) δ: 23.3, 57.8 (2 × CH_3), 23.8, 28.4, 67.8 (3 × CH_2), 66.5 (CH), 125.8, 134.0 (2 × HC=). Exact Mass calcd. for $C_7H_{12}O$ (M – 32): 112.0888; found: 112.0892.

1-Methyl-6-methoxy-cis-*4-hexenyl-2′-cyclopentadiene (10)*

To a stirred solution of **9** (1.44 g, 10 mmol) in dry pyridine (12 mL), at ice-bath temperature, was added *p*-toluenesulfonyl chloride (2.87 g, 15 mmol) in small portions. The reaction mixture was then stirred at 0°C for 2 h and placed in a refrigerator for 12 h. The mixture was neutralized with ice-cold 30% aqueous HCl solution before extraction with ether (3 × 30 mL). The combined extracts were washed with water, 3% aqueous HCl, 5% aqueous $NaHCO_3$ solution, and brine before drying over anhydrous $MgSO_4$. Removal of the ether gave the desired tosylate of **9** (2.85 g, 96%) as a thick oil; ir ($CHCl_3$): 3040 (=CH), 2835 (OMe), 1580 (Ph), 1440 (C=C), 1180 (-SO_3R) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 1.20 (d, 3H, J = J.6 Hz, H-1), 1.45–1.7 (m, 2H, H-3), 1.8–2.1 (m, 2H, H-4), 2.39 (s, 3H, aryl-Me), 3.25 (s, 3H, OMe), 3.83 (d, 2H, H-7), 4.56 (tq, 2H, J = 6.5, 7.5 Hz, H-2), 5.3–5.5 (m, 2H, H-5,6), 7.3, 7.7 (AA′BB′ system of aryl CH's); ^{13}Cmr ($CDCl_3$) δ: 20.7, 21.5, 57.9 (3 × CH_3), 23.1, 36.3, 67.9 (3 × CH_2), 79.8 (CH), 127.0, 131.5 (2 × CH=), 127.6, 129.7 (2 × 2 aryl CH), 134.4, 144.5 (2 × aryl C).

Sodium sand was prepared by vigorously stirring sodium metal (0.345 g) in refluxing xylene (20 mL) under nitrogen. The xylene was decanted and the sodium sand washed with THF (2 × 20 mL). To a stirred suspension of the sand in 10 mL of THF was added freshly distilled cyclopentadiene in several portions until the sodium was consumed (ca. 3h). The resulting deep red-purple solution was then cooled in an ice-bath. A solution of the tosylate (2.98 g, 1 mmol) in THF (10 mL) was added slowly over 30 min and the reaction mixture was stirred overnight. The resulting light brown mixture was diluted with brine and then extracted with ether (3 × 50 mL). The combined extracts were washed with brine before drying over anyhdrous $MgSO_4$. Evaporation of the solvent left a dark brown oil, which was purified by FC (Et_2O – petroleum ether, 10:90) to give **10** as a light yellow oil (1.60 g, 84%); ir ($CHCl_3$): 3060, 3025 (=CH), 2840 (OMe), 1450 (C=C), 1105 (C—O) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 1.06 (d, J = 6.8 Hz, 1-Me), 1.4–1.6 (m, H-2), 2.00 (m, H-3), 2.55 (m, H-1), 2.845 (m) and 2.925 (m) (int. ratio 3:5, =CCH_2C=′s), 3.28 (s, OMe), 5.4–5.6 (m, H-4, 5), 5.8–6.4 (m's, =CH's); ^{13}Cmr ($CDCl_3$) δ: (major component): 20.2, 57.7_6 (2 × CH_3), 25.4, 36.1, 40.9, 68.0 (4 × CH_2), 33.7 (CH), 124.8, 126.0, 133.0, 133.6, 133.7 (5 × =CH), 151.9 (sp^2-C); (minor component): 21.2, 57.8_1 (2 × CH_3), 25.4_6, 37.1, 40.6, 68.0 (4 × CH_2), 34.6 (CH), 125.6, 126.0, 130.4, 132.1, 133.4 (5 × =CH), 154.5 (sp^2-C). Exact Mass calcd. for $C_{13}H_{20}O$: 192.1514; found; 192.1514.

2-Methyl-exo-*6-methoxymethyltricyclo[5.2.1.0^{1,5}]dec-8-ene (**11**)*

Xylene (50 mL) was heated to reflux under nitrogen with stirring before the slow addition of triene **10** (1.92 g, 10 mmol) in xylene (50 mL) over the course of an hour. Heating under reflux was continued for 24 h before the xylene was removed under vacuum at 45–50°C (bath temperature) to furnish a dark oil. This Diels–Alder product was purified by FC (EtOAc – petroleum ether, 2.5:98.5) to give a 2:1 mixture of the 2-epimers of **11** (1.57 g, 82%) as a faintly yellow liquid, bp 90°C/0.2 Torr (Kugelrohr distillation; 1 Torr = 133.3 Pa); ir ($CHCl_3$): 3035 (=CH), 2820 (OMe), 1450 (C=C) cm^{-1}. ^{1}Hmr ($CDCl_3$) δ: (major epimer): 1.03 (d, 3H, J = 7.0 Hz, 2-Me), 2.70 (m, 1H, H-7), 3.31 (s, 3H, OMe), 3.2–3.35 (m, 2H, CH_2OMe), 6.03 ("t", 1 H, J ca. 6 Hz, H-8), 6.21 (d, 2H, J = 6.1 Hz, H-9); (minor epimer): 0.92 (d, 3H, J = 6.7 Hz, 2-Me), 2.70 (m, 1H, H-7), 3.27 (s, 3H, OMe), 6.08 (m, 2H, H-8,9); ^{13}Cmr ($CDCl_3$) δ: (major epimer): 20.0, 58.8, (2 × CH_3), 25.1, 37.2, 49.3, 75.6 (4 × CH_2), 32.5, 41.2, 46.1, 46.5 (4 × CH), 66.1 (quat C), 136.6, 138.1 (2 × CH=); (minor epimer): 17.2, 58.8 (2 × CH_3), 23.3, 34.8, 42.8, 75.6 (4 × CH_2), 33.3, 41.8, 46.3, 47.5 (4 × CH), 67.5, (quat C), 137.2, 140.3 (2 ×CH=). Exact Mass calcd. for $C_{13}H_{20}O$: 192.1514; found 192.1515.

2-Methyl-exo-*6-methoxymethyltricyclo[5.2.1.0^{1,5}]decan-8-one (**13**)*

To a stirred solution of BH_3·Me_2S (1.14 g, 15 mmol) in THF (30 mL) at 0°C under nitrogen was added 2-methyl-2-butene (2.1 g, 30 mmol) and stirring was continued at 0–10°C for 2 h. To this clear solution of $Siam_2BH$ was slowly added a solution of the tricyclic olefin **11** (0.96 g, 5 mmol) in THF (2 mL) over 20 min. Stirring was continued at 0° to –5°C for 4 h before the reaction mixture was left to stand with stirring overnight without cooling. The mixture was cooled as the excess $Siam_2BH$ was destroyed by the slow addition of cold water (0.4 mL) before the addition of 3 M aqueous NaOH (5 mL). Hydrogen peroxide (30%, 5.0 mL) was then added cautiously at room temperature and the mixture was allowed to stand for 24 h with stirring. After dilution with brine (20 mL), the reaction mixture was extracted with ether (3 × 45 mL). The combined extracts were washed with brine until neutral, 10% aqueous Na_2SO_3 solution (2 × 25 mL), and again with brine until the washings gave a negative peroxide test, before drying over anhydrous $MgSO_4$. Evaporation of the ether gave a viscous oil that was purified by FC (EtOAc – petroleum ether, 40:60) to yield alcohol **12** as a colorless, thick oil (0.81 g, 74%); ir ($CHCl_3$): 3630, 3470 (OH), 3020 (=CH), 2830 (OMe), 1465 (C=C), 1110 (C—O) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ (major epimer): 0.81 (d, 3H, J = 7.0 Hz, 2-Me), 3.1–3.24 (m, 2H, 6-CH_2O-), 3.25 (s, 3H, OMe), 3.85 (m, 1H, H-7); (minor epimer): 0.89 (d, 3H, J = 6.6 Hz, 2-Me); ^{13}Cmr ($CDCl_3$) δ (major epimer): 18.9, 58.6 (2 × CH_3), 23.8, 36.0, 36.4, 41.8, 73.8 (5 × CH_2), 33.6, 40.8, 47.9, 49.1, 75.2 (5 × CH), 58.9 (quat C); (minor epimer): 15.9, 58.6 (2 × CH_3), 22.6, 29.3, 34.4, 43.1, 73.8 (5 × CH_2), 34.3, 41.3, 49.1, 49.8, 75.3 (5 × CH), 60.3 (quat C). Exact Mass calcd. for $C_{13}H_{22}O_2$: 210.1619; found: 210.1623. A solution of **12** (0.21 g, 1 mmol) in CH_2Cl_2 (2 mL) was added to a stirred suspension of PCC (0.322 g, 1.5 mmol), NaOAc (0.028 g, 0.34 mmol), and Celite (300 mg) in CH_2Cl_2 (10 mL). This reaction mixture was stirred for 3.5 h at room temperature before the addition of ether and filtration through a short column of silica. The solvent was then evaporated and the residue purified by Kugelrohr distillation to yield **13** as a 2:1 mixture of 2-epimers (0.197 g, 95%), bp 110–115°C/0.2 Torr; ir ($CHCl_3$): 3040 (=CH), 2820 (OMe), 1740 (C=O), 1105 (C—O) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ (major epimer): 0.86 (d, 3H, J = 7.1 Hz, 2-Me), 3.24 (s, 3H, OMe), 3.2–3.3 (m, 2H, -CH_2O-); (minor epimer): 0.92 (d, 3H, J = 6.5 Hz, 2-Me), 3.24 (s, 3H, OMe); ^{13}Cmr ($CDCl_3$) δ (major epimer): 18.7, 58.5 (2 × CH_3), 24.2, 36.1, 39.1, 46.3, 72.6 (5 × CH_2), 34.5, 39.2, 47.8, 55.7 (4 × CH), 58.9 (quat C), 217.4 (C=O); (minor epimer): 15.6, 58.5, (2 × CH_3), 22.4, 32.8, 33.6, 46.9, 72.6 (5 × CH_2), 34.6, 40.0, 49.2, 55.3 (4 × CH), 60.0 (quat C), 217.5 (C=O). Exact Mass calcd. for $C_{13}H_{20}O_2$: 208.1463; found: 208.1463.

2-Methyl-exo-*6-methoxymethyltricyclo[5.3.1.0^{1,5}]undecan-8-one (**16**)*

A solution of **13** (208 mg, 1 mmol) in THF (1.0 mL) was added under N_2 at –70°C to a stirred solution of LDA (diisopropylamine (172 mg, 1.7 mmol), THF (2.5 mL), and *n*-BuLi (0.58 mL, 5.6 M in hexane) at –70°C, 20 min). Stirring at –70°C was continued for 1 h before the addition of quenching solution prepared by centrifugation of a mixture of TMSCl (333 mg, 3.1 mmol), Et_3N (42 mg, 0.42 mmol), and THF (1.0 mL) in a nitrogen-purged tube. After the reaction mixture was stirred at –70°C for another hour, it was allowed to warm to room temperature and, after 2 h, was diluted with saturated aqueous $NaHCO_3$ solution; the product was extracted with ether (3 × 25 mL). These extracts were washed with brine and then dried over $MgSO_4$. Removal of the solvent afforded a yellow oil that was purified by Kugelrohr distillation to yield colorless **14** as a mixture of 2-epimers (251 mg, 90%): bp 110°C/0.2 Torr; ir ($CHCl_3$): 3060 (=CH), 2820 (OMe), 1625 (C=C), 1105 (C—O), 860 ($SiCH_3$) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ (major epimer): 0.15 (s, 9H, $SiMe_3$), 0.95 (d, 3H, J = 6.6 Hz, 2-Me), 3.30 (s, 3H, OMe), 3.25–3.40 (m, 2H, -CH_2O-), 4.87 (d, 1H, 0.6 Hz, H-9); (minor epimer): 0.15 (s, 9H, $SiMe_3$), 0.90 (d, 3H, J = 6.0 Hz, 2-Me), 3.30 (s, 3H, OMe), 4.68 (d, 1H, J = 0.6 Hz, H-9); ^{13}Cmr ($CDCl_3$) δ (major epimer): 0.0 (3), 19.9, 58.8 (5 × CH_3), 24.9, 36.3, 47.7, 75.4 (4 × CH_2), 33.2, 40.8, 48.9, 50.4, 107.6 (5 × CH), 65.1, 161.7 (2 × C); (minor epimer): 0.0 (3), 16.9, 58.8 (5 × CH_3), 23.1, 34.3, 41.2, 75.4 (4 × CH_2), 33.8, 41.4, 50.1, 50.6, 109.2 (5 × CH), 66.3, 161.9 (2 × C). Exact Mass calcd. for $C_{16}H_{28}O_2Si$: 280.1859; found: 280.1861.

Methylene iodide (456 mg, 1.7 mmol) was added to Zn/Ag couple (195 mg, 3.0 mmol) in ether (1.0 mL) and the mixture was warmed until refluxing occurred without external heating. When refluxing ceased, more ether (0.5 mL) was added and the mixture stirred for 1 h at room temperature. Trimethylsilyl enol ether **14** (280 mg, 1.0 mmol) in Et_2O (1.5 mL) was added and the mixture was heated under gentle reflux overnight. After cooling to 0°C, pyridine (320 mg, 4.05 mmol) and pentane (7.0 mL) were added with vigorous stirring. The precipitate that formed was removed by filtration and washed several times with pentane. The combined washings were concentrated at room temperature to furnish a light yellow oil which, upon FC (Et_2O – petroleum ether, 20:80), gave the cyclopropanated **15** as a colorless oil (237 mg, 81%); ir ($CHCl_3$): 3050 (cyclopropyl CH), 2820 (OMe), 1100 (C—O), 860, 840 (C—O—Si) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.11 (s, 9H, $SiMe_3$), 0.45–0.95 (m, 3H, cyclopropyl H's), 0.92 (d, 3H, J = 7.0 Hz, 2-Me), 3, .29 (s, 3H, OMe); ^{13}Cmr ($CDCl_3$) δ (major): 0.9 (3), 19.4, 58.5 (5 × CH_3), 10.5$_4$, 24.0, 32.5, 36.6, 74.2$_5$ (5 × CH_2), 22.3, 33.0, 40.2, 47.1, 49.3 (5 × CH), 60.2, 60.7 (2 quat C); (minor): 0.9 (3), 16.5, 58.5 (5 × CH_3), 10.5, 22.2, 25.6, 34.1, 74.3 (5 × CH_2), 24.4, 35.1, 40.3, 46.8, 50.5 (5 × CH), 60.2, 60.6 (2 quat C). Exact Mass calcd. for $C_{17}H_{30}O_2Si$: 294.2015; found: 294.2011.

To a solution of **15** (294 mg, 1.0 mmol) in MeOH (2.1 mL), stirring at 0°C, was added 0.42 mL of 3 M aqueous NaOH solution. Stirring was continued for 3 h before the mixture was allowed to stand in the refrigerator for 24 h. After removal of the methanol at 40°C under vacuum, the mixture was diluted with brine (5 mL) and extracted with ether (4 × 5 mL). The combined extracts were washed with brine before drying over anhydrous $MgSO_4$. Evaporation of the solvent gave a faintly yellow oil, which upon FC (Et_2O – petroleum ether, 40:60) furnished the desired tricyclic ketone **16** (194 mg, 88%) as a 2:1 mixture of the 2-epimers; ir ($CHCl_3$): 1700 (C=O), 1090 (C—O) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.85 (d, 3H, J = 7.0 Hz, 2-Me), 2.55 (bd, 1H, J = 5 Hz, H-7), 3.22 (s, 3H, OMe), 3.15–3.35 (m, 2H, -CH_2O-); ^{13}Cmr ($CDCl_3$) δ (major epimer): 16.3, 58.5 (2 × CH_3), 25.2, 32.0, 35.4, 36.1, 41.7, 73.1 (6 × CH_2), 40.1, 43.2, 49.8, 57.1 (4 × CH) 53.9 (quat C), 213.2 (C=O); (minor epimer): 14.7, 58.5 (2 × CH_3), 23.3, 33.8, 33.9, 34.7, 36.0, 73.1 (6 × CH_2), 40.9, 44.5, 48.7, 55.6 (4 × CH), 56.1 (quat C), 213.4 (C=O). Exact Mass calcd. for $C_{14}H_{22}O_2$: 222.1620; found: 222.1617.

*2,9,9-Trimethyl-6-methoxymethyltricyclo[5.3.1.0^{1,5}]undecan-8-one (**6**)*

Ketone **16** (222 mg, 1.0 mmol) in Et_2O (1 mL) was added dropwise to a vigorously stirred suspension of $NaNH_2$ (211 mg, 5.4 mmol) in Et_2O (2.5 mL) at room temperature under nitrogen and the mixture was refluxed gently with stirring for 3.5 h before cooling to room temperature. Methyl iodide (0.4 mL, 6.5 mmol) was slowly added and the

reaction mixture was refluxed overnight with vigorous stirring. After a second addition of methyl iodide (0.14 mL, 2.25 mmol), the mixture was refluxed for an additional 2.5 h before cooling to room temperature. Water (2 mL) was added and the product extracted with ether (3 × 15 mL). The combined extracts were washed with brine and then dried over anhydrous $MgSO_4$. After removal of the solvent, the product was purified by Kugelrohr distillation to yield **6** as a 2:1 mixture of epimers (201 mg, 80%): bp 120–125°C/0.1 Torr; ir ($CHCl_3$): 1700 (C=O), 1105 (C—O) cm^{-1}; ^{1}Hmr ($CDCl_3$) δ (major epimer): 0.85 (d, 3H, J = 7.2 Hz, 2-Me), 1.07 (s, 3H, 9-Me), 1.12 (s, 3H, 9-Me), 3.25 (s, 3H, OMe), 3.15–3.35 (m, 2H, -CH_2O-); (minor): 0.86 (d, 3H, J = 6.5 Hz, 2-Me), 1.07 (s, 3H, 9-Me), 1.12 (s, 3H, 9-Me), 3.24 (s, 3H, OMe); ^{13}Cmr: see Table 3. Exact Mass calcd. for $C_{16}H_{26}O_2$: 250.1933; found: 250.1926.

*Alcohol (**19**)*

A sample of the epimeric mixture **6** (20 mg, 0.08 mmol) in Et_2O (1 mL) was slowly added to a cooled suspension of LAH (10 mg, 0.25 mmol) in Et_2O (2 mL). After the addition, the mixture was stirred at room temperature for 1 h before the cautious addition of a few drops of water to destroy excess LAH. The mixture was acidified with 5% aqueous HCl (2 mL) and the product extracted with ether. The extracts were washed with saturated $NaHCO_3$ solution, brine, and water before drying over anhydrous $MgSO_4$. Evaporation of the ether afforded lightly colored **19** (18.5 mg, 91%); ir (film): 3550 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.82 (d, 6H, J = 6.8 Hz, 2-Me), 0.990 (s, 6H, 9-Me, major), 1.012 (s, 6H, 9-Me, minor), 3.1–3.3 (m, 4H, 2 × -CH_2O-), 3.28 (s, 6H, 2 ×MeO), 3.45 (m, 2H, 2 × -CH(OH)-); ^{13}Cmr: see Table 3. Exact Mass calcd. for $C_{16}H_{28}O_2$: 252.2089; found: 252.2094.

*2,9,9-Trimethyl-6-methylenetricyclo[5.3.1.0^{1,5}]undecan-8-one (**20**)*

Sodium iodide (270 mg, 1.8 mmol) was added to a solution of the epimeric mixture **6** (433 mg, 1.7 mmol) in dry acetonitrile (10 mL) under argon. A solution of trimethylsilyl chloride (0.7 mL, 600 mg, 5.4 mmol) in CH_3CN (0.7 mL) was very slowly added with stirring. As the reaction proceeded a yellow color developed and gradually intensified. The progress of the reaction was monitored at 0.5 h intervals by tlc and, after 3 h, the starting material had been consumed. The reaction mixture was diluted with water and extracted with ether. The combined extracts were washed with 10% aqueous $NaHCO_3$ solution, 10% sodium thiosulfate solution, water, and brine before drying over $MgSO_4$. Removal of the solvent gave a crude product that was purified by FC (Et_2O – hexane, 20:80) to give the expected 6-iodomethylene derivative (395 mg, 67%) and the analogous alcohol (80 mg. 20%), both as 2:1 epimeric mixtures. These were identified by ^{13}Cmr; the spectrum of the iodides had distinctive signals near δ_C 8 for the -CH_2I groups.

*2-Methyl-6-iodomethyl-**4***: ir (film): 1705 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.85 (d, 3H, J = 6.7 Hz, 2-Me minor), 0.88 (d, 3H, J = 7.0 Hz, 2-Me major), 1.121 (s, 6H, 9-Me), 1.165 (s, 6H, 9-Me), 3.0–3.3 (m, 6-CH_2I); ^{13}Cmr ($CDCl_3$) δ (major epimer): 16.4, 31.5$_1$, 31.5$_4$ (3 × CH_3), 8.2$_7$, 24.7, 35.8, 37.9, 46.5 (5 × CH_2), 41.4, 47.8, 50.0, 59.7 (4 × CH), 42.2, 55.5 (2 × C), 217.1 (C=O); (minor epimer): 14.6, 31.3, 31.4$_6$ (3 × CH_3), 8.2$_3$, 23.3, 30.3, 33.1, 42.2 (5 × CH_2), 41.3, 48.8, 49.9, 58.4 (4 × CH), 42.5, 57.1 (2 × C), 217.4 (C=O).

*2-Methyl-6-hydroxymethyl-**4***: ir (film): 1703, 3443 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.874 (d, 3H, J = 7.1 Hz, 2-Me major), 0.886 (d, 3H, J = 6.6 Hz, 2-Me minor) 1.107 (s, 6H, 9-Me), 1.155 (s, 6H, 9-Me), 3.4–3.7 (m, -CH_2O-); ^{13}Cmr ($CDCl_3$) δ (major epimer): 16.3, 31.4, 31.5 (3 × CH_3), 24.8, 35.9, 38.4, 46.8, 63.4 (5 × CH_2), 40.9, 46.6, 48.3, 55.8 (4 × CH), 42.2, 54.8 (2 × C), 218.7 (C=O); (minor epimer): 14.6, 31.2, 31.3 (3 × CH_3),23.3, 30.8, 33.2, 49.1, 63.1 (5 × CH_2), 40.9, 47.6, 48.2, 54.6 (4 × CH), 42.5, 56.6 (2 × C), 219.0 (C=O).

Under dry nitrogen, a 1 M solution of potassium *tert*-butoxide in anhydrous *tert*-butyl alcohol (2 mL) was added to the mixture of iodides (312 mg, 0.9 mmol) and the solution was stirred at 50°C for 2 h, after which time tlc indicated that the iodide had been consumed. The mixture was diluted with water and the product extracted with ether. The combined extracts were washed with cold water until neutral, then with brine before drying over $MgSO_4$. Evaporation of the solvent afforded a colorless oil (184 mg, 94%) that gave ^{13}Cmr spectra (Table 3) that were identical to those obtained for **20**, isolated from the neutral homoenolization product; ir (liquid film): 1700 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.849 (d, 3H, J = 7.0 Hz, 2-Me major), 0.857 (d, 3H, J = 6.7 Hz, 2-Me minor), 1.064 (s, 6H, 9-Me), 1.096 (s, 6H, 9-Me), 4.80 and 5.05 (multiplets, =CH_2). Exact Mass calcd. for $C_{15}H_{22}O$: 218.1671; found: 218.1674.

Homoenolization experiments

Our standard procedures for homoenolization experiments (32) were followed as outlined for **6**. To a solution of *t*-BuO–/*t*-BuOH (1.27 M, H_2O content <250 μg/mL) was added **6**, to obtain a solution that was 0.26 M in ketone. Aliquots (0.35 mL) were transferred to a series of 5-mL predried, thick-walled glass tubes; these tubes were then degassed and sealed before immersion in a Blue M constant high-temperature oil-bath at 185 ±1°C. These tubes were removed after intervals of several hours, cooled before opening, and the contents collected by washing with water and pentane. The neutral organic products were isolated by pentane extraction (3 × 15 mL) and the combined extracts dried over anhydrous magnesium sulfate. The aqueous layer was acidified with 10% aqueous HCl solution (10 mL) before ether extraction (3 × 15 mL) to recover any acidic organic products. The combined ether extracts were dried over magnesium sulfate.

To identify the acidic products, the oily residue obtained upon removal of the ether was examined by ^{13}Cmr. These data led to structure **22**, as described in the text; ^{1}Hmr ($CDCl_3$) δ (major epimer): 0.878 (d, 3H, J = 6.4 Hz, 6-Me), 1.148 (s, 3H, 2′-Me), 1.18 (s, 3H, 2′-Me), 1.56 (bs, 3H, 2-Me), δ1.47 (m, 1H, H-6), 1.417 (d, 1H, J = 14.6, Hz, H-1′), 1.887 (d, 1H, J = 14.6 Hz, H-1′), 2.01 (dm, 1H, J = 16.5 Hz, H-4), 2.199 (dm, 1H, J = 16.5 Hz, H-4), 2.56 (bd, 1H, J δ 9 Hz, H-1), 4.94 (m, 1H, H-3); (minor epimer): 0.837 (d, 3H, J = 6.6 Hz, 6-Me), 1.18 (s, 3H, 2′-Me), 1.206 (s, 3H, 2′-Me), 1.56 (bs, 3H, 2-Me), δ 1.67 (m, 1H, H-6), 1.711 (d, 1H, J = 14.7 Hz, H-1′), 1.968 (d, 1H, J = 14.7 Hz, H-1′), 1.819 (dm, 1H, J = 17 Hz, H-4), 2.219 (dm, 1H, J = 17 Hz, H-4), 2.61 (bd, 1H, J δ 9 Hz, H-1), 5.06 (m, 1H, H-3); ^{13}Cmr: see Table 4. Exact Mass calcd. for $C_{15}H_{24}O_2$: 236.1776; found: 236.1770.

*3,3,8,11-Tetramethyl[3.3.3]propell-8-en-2-one (**25**)*

The neutral product exhibiting the shortest retention time on glc analysis was assigned structure **25** as discussed in the text; ir (liquid film): 1730 cm^{-1}; ^{1}H and ^{13}Cmr data are listed in Table 5. Exact Mass calcd. for $C_{15}H_{22}O$: 218.1671; found: 218.1670.

*2,6,9,9-Tetramethyltricyclo[5.3.1.0^{1,5}]undec-5-en-8-one (**21**)*

The second band found by glc analysis was assigned structure **21** as discussed in the text; ir (liquid film): 1701 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.86 (d, 3H, J = 7.0 Hz, 2-Me minor), 0.88 (d, 3H, J = 6.5 Hz, 2-Me major), 1.12 (s, 6H, 9-Me), 1.13 (s, 6H, 9-Me), 1.56 (bs, 3H, 6-Me major), 1.57 (bs, 3H, 6-Me minor), 2.95 (bm, 1H, H-7); the ^{13}Cmr data are collected in Table 3. Exact Mass calcd. for $C_{15}H_{22}O$: 218.1671; found: 218.1674.

*2,6-Dimethyl-5-(3′-hydroxy-2′,2′-dimethylpropyl)bicyclo[3.3.0]oct-2-ene (**24**)*

The fourth glc band was found to contain a mixture of alcohols that was shown to be **24** as noted in the text; ir (liquid film): 3355 cm^{-1}; ^{1}Hmr ($CDCl_3$) δ: 0.85 (d, 3H, J = 6.2 Hz, 6-Me minor), 0.87 (d, 3H, J = 6.6 Hz, 6-Me major), 0.927 (s, 12H, 2′-Me), 1.61 (bs, 6H, 2-Me), 5.03 (m, 1H, H-3 minor), 5.15 (m, 1H, H-3 major); ^{13}Cmr: see Table 4. Exact Mass calcd. for $C_{15}H_{26}O$: 222.1981; found: 222.1981.

*3,3,11-Trimethyl-7-methoxymethyltricyclo[6.3.0.0^{1,5}]undecan-4-one (**7**)*

The fifth glc band was assigned structure **7** on the basis of its physical data; ir (liquid film): 1730 cm^{-1}; ^{1}Hmr: see text; ^{13}Cmr: see Table 2. Exact Mass calcd. for $C_{16}H_{26}O_2$: 250.1933; found: 250.1935.

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